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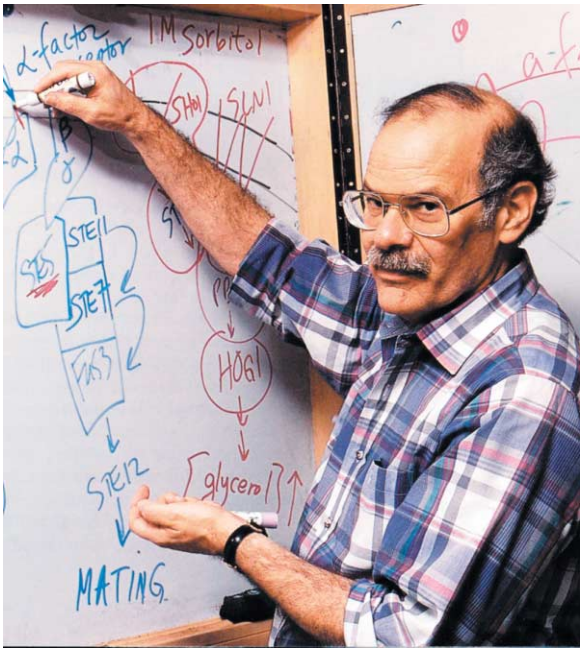
Obituary

Ira Herskowitz (1946–2003)



Ira Herskowitz

Photo courtesy of Kay Chernush.

On June 27, two months after Ira Herskowitz's death from cancer, more than 300 of his family, friends, and colleagues gathered at the Legion of Honor in San Francisco to reflect on Ira's remarkable life. The memorial, like Ira himself, celebrated science, music, and the art of mentoring, and it reminded us that, even in today's competitive climate, straight talk combined with a generous spirit is compatible with accomplishment and recognition.

Ira and his identical twin, Joel, were born in 1946 in Brooklyn to parents Reida and Irwin. They attended high school in Missouri, while their father, a *Drosophila* geneticist, was a member of the Genetics Department at St. Louis University.

Ira was an undergraduate at Caltech where his interactions with Jean Weigle and Sandy Parkinson directed him toward bacteriophage λ as a system for gaining insight into developmental processes. After graduating in 1967, Ira continued studies of developmental phage genetics at MIT with Ethan Signer. Ira's PhD thesis (1971) "Control of late genes, early genes, the cI gene, and replication in bacteriophage λ" revealed, by its very title, both the breadth and the intensity of Ira's interests. It also revealed his modus operandi: using simple genetics to ask and answer big questions.

In 1971, in his last year of graduate school, Ira accepted an Assistant Professorship in the University of Oregon's Institute of Molecular Biology, deferring his arrival to spend a year at MIT with David Botstein to gear up for work on yeast. At Eugene, Ira continued his passionate interest in λ lifestyle decisions—studying how λ determined whether to lyse its host or reside peacefully within it. He also began his study of how yeast makes lifestyle decisions, choosing as his entry point a most important issue—cell type specification. How do yeast decide to switch from the **a** cell type to the α cell type so that mating can occur? His incisive genetic experiments suggested a novel mechanism—insertion of a new cassette with opposite mating type information. In 1977, the significance and potential of that work was recognized by Jim Watson, who convinced two of Ira's earliest students (Jeff Strathern and Jim Hicks) to join with Amar Klar to create a year-round program in yeast genetics at Cold Spring Harbor. Among the accomplishments of this Cold Spring Harbor Yeast group, which attracted the best and brightest of young collaborators, was the demonstration that mating type interconversion was achieved by genetic recombination, initiated by a DNA double-strand break.

In 1981, Ira was enticed to move to San Francisco, where he remained for the rest of his life. At UCSF, he continued to study cell type specification, dissecting the molecular circuits responsible for mating type switching. He also broadened his sphere of inquiry. He investigated morphogenetic questions, determining how bud sites are selected and cell polarity established, touched on signal transduction by studying crosstalk between pathways, and examined sporulation as a developmental program. Recently, Ira began using yeast to directly learn about human genetics, performing a "proof of principle" study showing that yeast and mammals share similar mechanisms of resistance to the anticancer drug cisplatin. Finally, Ira developed a new love—pharmocogenomics. Stymied by the inability to carry out genetic experiments in humans, Ira spearheaded a study of whether inherited differences in membrane transporters correlated with altered response to drugs.

Ira was an inspiring scientist with a generous heart. His hallmark was the ability to use simple genetics, supplemented in later years by the judicial application of molecular biological, genomic, and bioinformatic tools, to ask big questions. His genius was his ability to look at the data and formulate elegant hypotheses, often with universal implications.

His driving force was an intense desire to understand the workings of life and derive the truth, almost akin to the drive of a Talmudic scholar. In this pursuit, he cared little whether it was his idea or someone else's that provided the key to understanding. As Ira never failed to acknowledge the contributions of others, both competitors and collaborators were drawn together in the search for understanding. It is completely in character that Ira orchestrated the award of the 2001 Thomas Hunt Morgan Medal to Yasuji Oshima (Herskowitz and O'Shea, 2002) so that Oshima's contributions to mating type switching would be forever acknowledged.

Not surprisingly, Ira was also an inspiring mentor, able to instill in his associates both a big approach to science and an appreciation of hypotheses, while facilitating the development of their own personal styles. His success was astounding. Many continued working on problems started in his lab. Others used the approaches learned from Ira to tackle new organisms or problems.

Ira's dedication to science education was manifested in both imaginable and unimaginable ways. Who could forget Ira's whimsical, but highly informative, pictorial summary of λ's control circuits (shrink-wrapped with the 1983 Cold Spring Harbor volume Lambda II)? Or Ira's guitar/vocal performances of Joel's "Double Talking Helix Blues" (available from Cold Spring Harbor Laboratory Press)? In review articles, he presented his understanding of λ and yeast development and their wider applications to a grateful community (Herskowitz, 1973, 1987, 1989, 1997; Herskowitz and Hagen, 1980), which rewarded him with the National Academy of Sciences Award for Excellence in Scientific Reviewing in 1985. As course director of Genetics at UCSF for eighteen years, Ira's success in instilling generations of graduate students (and their faculty mentors) with awareness of the "awesome power of yeast genetics" was legendary. His impact can be measured by the fact that hardly a single UCSF laboratory, regardless of research orientation, was immune to the logic of this approach.

More than anyone else we know, Ira's spirit combined competition with generosity. To illustrate—upon his arrival in Eugene, Ira quickly scooped up all graduate students who had not yet chosen labs (and some who had). The brain-drain suffered by less talented faculty was more than compensated for by the help Ira gave us—from advice on the nitty-gritty of phage and yeast development to a vision of the future for our program. And we all enjoyed watching this brilliant, interactive Pied Piper rapidly achieve worldwide scientific recognition with one hand, while beating us at ping-pong with the other. When Ira left Eugene, he cried and so did we.

Ira was equally valued in San Francisco, where students and postdocs vied to join his laboratory or to secure him as a member of their thesis committee, and faculty relied upon him for incisive suggestions and for leadership in new directions. When Ira died, UCSF mourned the loss of one of its anchors. But the students said it best. Although policies of the University of California may prevent it from happening, a remarkable document from the UCSF graduate students asked that a building at Mission Bay be named Herskowitz Hall "in memory and remembrance of a truly inspiring and excellent member of the UCSF family. His overall presence, ranging from whistling down the hall to teaching Genetics to singing the DNA Blues, are memories that have touched us all forever. We would like to see this wonderful person honored in such a way that his spirit lives on forever at UCSF. He was the heart and soul of the UCSF community."

Sentiments of Ira's colleagues at Eugene and UCSF were widely shared. By the time Ira died at the age of 56, he was an elected member of the Institute of Medicine, the National Academy of Sciences, and the American Academy of Arts and Sciences, and he had been honored by a MacArthur Fellowship, an Eli Lilly Award in Microbiology and Immunology, a Genetics Society of America Medal, a Thomas Hunt Morgan Medal for Lifetime Contribution to Genetics, and a Rosenstiel Award.

Ira Herskowitz

Photo courtesy of Kathy Giacomini.

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Selected Reading

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